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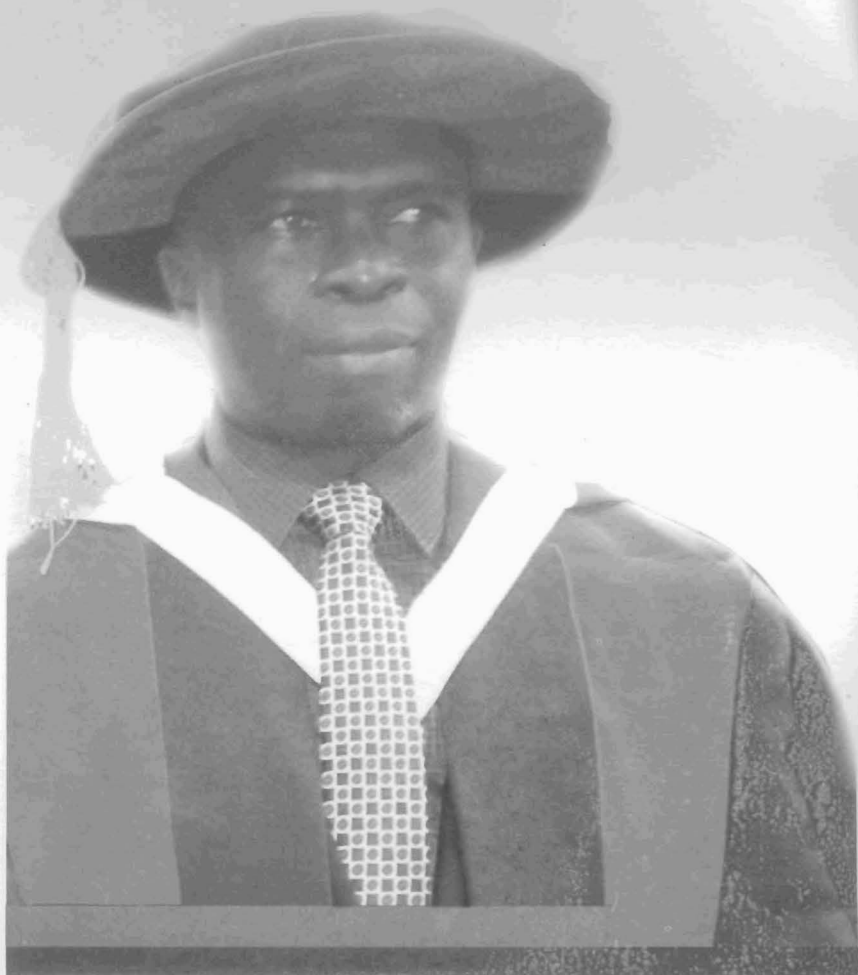
**PRAISING THE DEAD THAT  
ARE ALREADY DEAD**

By

**Prof. K.A. Adelusola**  
*Professor in Morbid Anatomy*



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# **PRAISING THE DEAD THAT ARE ALREADY DEAD**

**An Inaugural Lecture Delivered at Oduduwa Hall,  
Obafemi Awolowo University, Ile-Ife, Nigeria  
on Tuesday 11th June, 2013**

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**Inaugural Lecture Series 258.**

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The Vice Chancellor Sir,  
Have I not reason, beldams as you are,  
Saucy and overbold? How did you dare  
To trade and traffic with Macbeth  
In riddles and affairs of death,  
And I the mistress of your charms, .  
The close contriver of all harms,  
Was never called to bear my part,  
Or show the glory of our art? (Hecate meeting with the three  
witches in Macbeth).

This is a segment of the monologue of Hecate, the queen of the three witches, and the principal principality and power in Shakespeare's Macbeth.

Mr. Vice Chancellor sir, distinguished ladies and gentlemen today's inaugural lecture focuses on the riddles and affairs of death, and life. No one is more qualified to pontificate on those issues than the morbid anatomist himself. In other words, we are here this evening to hijack that monologue and that claim to mastery in the affairs of death from the mistress of the three witches in a scientific manner.

The Lord Jesus invited a man whose father had just died to follow him. The man asked for permission to first go and bury his deceased father before following Jesus. Jesus' reply was "let the dead bury their own dead." The people He was referring to as "the dead" were still alive. This means that one can be dead while still alive.

"Wherefore I praised the dead that are already dead, more than the living, which are yet alive" (King Solomon – Eccles 4:2)

Here again we see that some dead are already dead, while some are still living. The subject of this lecture is not about the dead that is still alive, but the one that is already dead, i.e. the biologically dead. But what is biological death? To answer this question we have to ask ourselves firstly what is life?

Life in biological context is characterised by:

- Maintenance of structure and function in a particular environment.
- Production and consumption of energy (metabolism).
- Growth and reproduction.
- Performance of active movement (work/locomotion).
- Ability to react to a stimulus (irritability).

Death is the cessation of life and all vital functions. Somatic death refers to death of the body as a whole. Molecular death is the death of cells, tissues and organs. Both somatic and molecular deaths may be referred to as biological death. Death may be from old age. In some cases, death is a result of disease in the body.

## **Disease in Antiquity**

Most deaths are as a result of disease in the body. According to Greek mythology illness arose as a result of the disobedience of Theodore Pandore. In ancient times health and disease were expressed in supernatural terms. There was little or no understanding about medical illness and treatment of diseases. Human beings were thought of as subjects to the will of gods and demons. Disease was considered to be caused by angry gods or demons. These interpretations were often seen in relation to moral behaviour. Because of their belief in the origin of disease the early physicians were diviners and priests. Treatment by magic and incantations against demons was the rule. Protection was sought by means of invocation and casting out of spirits, and the performance of spells and rituals. The belief that diseases are consequences of bad behaviour is deeply rooted in man. The disciples of Jesus Christ asked a pertinent question: who did sin that this man was born blind? There is support for the association of disease with moral behaviour in modern medicine.

1. The association of smoking with lung cancer.
2. The association of promiscuity with the human papilloma virus infection, cervical cancer, human immunodeficiency virus (HIV) infection and the acquired immune deficiency syndrome (AIDS).
3. The association of alcoholism with liver cirrhosis.
4. The association of smoking and alcohol abuse with oesophageal cancer.

It is sad to note that in this 21<sup>st</sup> century some Nigerians still submit themselves to the whims and caprices of diviners and demons. In other words the era of demonic medicine is still very much alive with us.

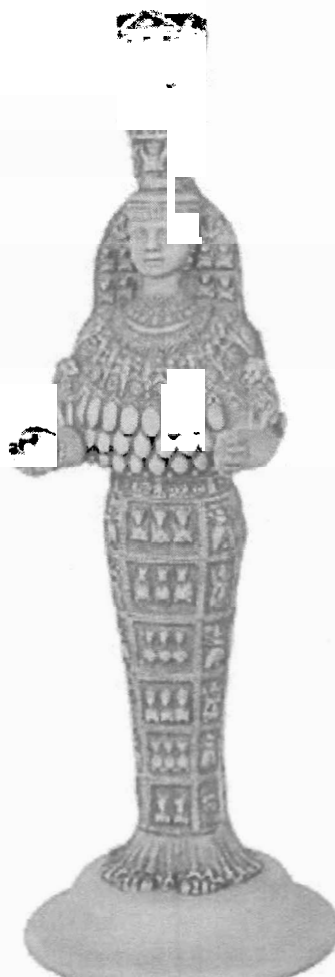
As time went by there was a paradigm shift and magic medicine gave way to more rational thinking and the emergence of humoral medicine. Hippocrates and Galen were the main proponents of this view. The human body was thought to consist of blood, phlegm, yellow bile and black bile. Through these he feels pain or enjoys health. Illness was caused by imbalance between the four components. Galen began study of medicine at the age of 16 years. He was physician first to gladiators, then to rich and powerful Romans. He was the main source of medical knowledge in the middle ages. Galenic theory dominated European medicine for close to 1500 years mainly because that was the view also shared by the Church of the middle age. The theory also dominated Jewish and Arabic thinking long after the death of Galen. Medicine at this time was practiced by monks. The Church invoked one or more saints for every illness. For example, prayer was made to Saint Vitus for relief from chorea, the cause of involuntary spasmodic movements, which became known as Saint Vitus' dance. Similarly, prayer was made to Saint Anthony for relief from ergotism, known as Saint Anthony's fire. Galenic theory remained unchallenged until Andreas Vesalius arrived at the scene in the 16<sup>th</sup> century. Galen's anatomy was based on animal dissection, which led to many errors. His physiology was also based on the philosophy of Plato and Erasistratus.

Early Greek medicine was also dominated by the concept that the gods caused disease. Various temples and cults existed where cure was by incantation, baths, sacrifices, diet and herbal medicine. Pergamum for example was the center of four pagan cults (Zeus, Athena, Dionysus and Esclepius). No wonder it was described as "where satan's seat is". Esclepius (or Asclepius) was a major cult at this period and it continued to be relevant up till the time of the Roman Empire. Esclepius was a deity associated with healing and medicinal arts. The rod of Esclepius is a serpent entwined and wielded by the Greek god. In recent times, it is associated with medicine and health. Similarly, Diana of Ephesus, a fertility goddess with accessory breasts all over the body was worshipped by the Ephesians. Relic of Diana of the Ephesians could be found today at the temple of Artemis in Turkey. This temple was one of the seven wonders of the ancient world.

The last traces of the humoral theory appeared in a book by eminent pathologist Karl von Rokitanski. The book was strongly condemned by the father of cellular pathology, Rudolf Virchow in a way that no one dared speak of humoral theory again.



**Rod of Asclepius**



**Goddess Diana of Ephesus**



But what are the beliefs of the Yoruba of South Western Nigeria about diseases and their origins? In his book titled *African Traditional Medicine: Practices Among the Yoruba of Nigeria* Professor D.D.O. Oyebola of the College of Health Sciences, Obafemi Awolowo University (OAU), opined that the Yoruba are aware that certain illnesses have natural or physical causation. They are aware for instance that inappropriate food can cause diarrhoea, stomach ache and other forms of diseases. Illnesses that are serious, protracted, sudden or extraordinary are believed to be caused by supernatural forces. The witch or sorcerer is believed to be responsible for such illnesses. It is believed that such evil people can worsen the course of a hitherto natural disease. Difficult labour, chronic mental illnesses and persistent failure in important life ventures are sometimes believed to be caused by witches or sorcerers.

### **The Pandora's Box**

According to Greek mythology, Pandora was the first woman on earth. When Prometheus stole fire from heaven, Zeus punished her by presenting a beautiful box (some say a jar) containing all manner of evil and diseases to Pandora with a strict instruction not to open the box. Propelled by curiosity, Pandora eventually opened the box releasing out all the evils and sicknesses into the world. Realising this, Pandora quickly closed the box but it was too late, only hope was left in the box.

### **Morbid Anatomy in History**

While we all owe our existence to the mercy of God Almighty, some people paid for the medical knowledge that enabled doctors understand the mechanism of disease and their effects on the body. These are the dead that are already dead. People are still dying and new diseases continue to emerge and by implication, knowledge about diseases from post mortem is on-going. In the beginning, Plato's idealist philosophy was becoming increasingly pervasive, especially among mathematicians and some natural philosophers. According to Plato, only the soul was sacred, not the body. The

physical body was mere appearance. Based on this philosophy, dissection of the body was permitted in Alexandria. Alexandria with nearly 70,000 scrolls was one of the greatest centers of learning during the classical period. Scholars such as Euclid, Archimedes, Herophilus passed through Alexandria. Herophilus and his pupil Erasistratus soon started performing dissection on the body of criminals from the king's prisons. Thus, some secrets of the human body were discovered. However, it remains a matter of speculation whether Herophilus and Erasistratus performed autopsy on dead criminals or on criminals whilst the breath of life remained in them. The death of Erasistratus by suicide c250BC put an end to dissection of human bodies for millennia. Dissection of the human body was forbidden. Animal anatomy took the centre stage.

Arabic medicine at this time was dominated by Haly ben Abbas and his successor Avicenna, the chief physician to the Baghdad hospital. The history of disease and medicine at that era will not be complete without mentioning Al-Razi and Avicenna. Al-Razi was the Chief physician at the Baghdad hospital. Among other accomplishments, he was the first to write about children's diseases. He believed there was no place for religion in science.

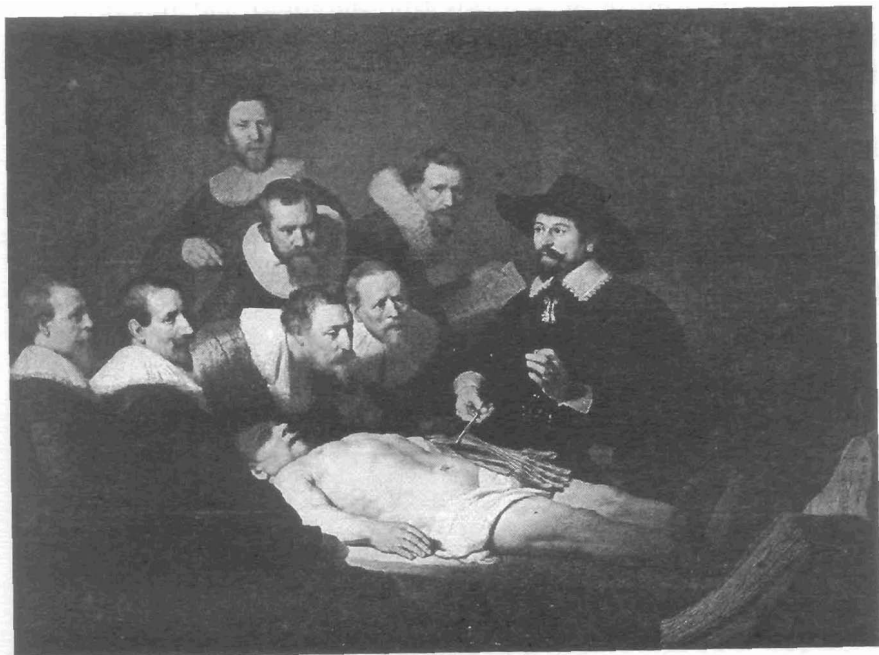
Avicenna (Ibn Sina) – physician, philosopher and scientist was one of the greatest philosophers of medieval period and the golden age of Islamic tradition. Others in this category were al-Farabi and Ibn Rashd. However, Avicenna remained the finest genius of Arabic medicine. To his students he was the al-Sheik-al-Rais (Leader among the wise men). Avicenna wrote extensively on metaphysics and his philosophical works were one of the main targets of al-Ghazali's attack on philosophical influence in Islam. Avicenna in the western world was known as the "Prince of the Physicians" for his famous medical text known as al Qanun, also called Canon of Medicine. This was the main medical text in European universities for centuries. His works influenced many Christian philosophers, notably Thomas Aquinas. Today, Canon of Medicine is domiciled at the P.I. Nixon Medical Historical Library, University of Texas Health Center at San Antonio. How it got there is anybody's guess.

Surprisingly, Avicenna was a prolific drinker and womaniser. The human body, to him was sacred and sacrosanct. He discouraged the practice of anatomical dissection and invasive surgery. He downgraded surgery as a practice that is manual rather than mental.

Welcome to the early 16<sup>th</sup> century, and here comes Andreas Vesalius, the author of the finest anatomy book in medical history. After studying at the University of Paris under Jacob Sylvius, Vesalius rose to become a professor of anatomy at the University of Padua at the age of 23 years. In his own account, he performed anatomical dissection on bodies taken from graves and bodies given to him after public execution. However, his description of specific female organs was weak, probably due to lack of executed female criminals. This deficiency was rectified by his student Gabriele Fallopius, who described in detail the female genital organs and named the fallopian tube after himself. Although Andreas Vesalius described many anatomical structures, he greatly erred by not naming a single structure after himself. He merely gave them Latin, Greek or Jewish names, a mistake his successor Fallopius avoided.

The discovery of the circulation of blood by William Harvey in the early 17<sup>th</sup> century marked the beginning of modern medicine. In his time, the professional body of London anatomists were permitted by act of Parliament to dissect the bodies of just four hanged criminals per year. Even in his lifetime he was recognised as the founding father of physiology, the scientific understanding of how the body actually works. His epic book "De Mortu Cordis" (1628) is one of the greatest books produced by an Englishman. Three other great books were also produced around this time: the Folio Edition of Shakespeare's plays (1623), the King James Authorised Version of the Holy Bible (1611) and also the highly technical book Principia mathematica (1687) authored by Sir Isaac Newton, a professor of mathematics at the University of Cambridge.

Later came the era of medical enlightenment. Before then the microscope had just been invented and scientists for the first time had the opportunity of peeping into the hitherto unseen world of microbes. Among the notable scientists of this period was Giovanni Morgagni, the founder of clinical pathology. Morgagni studied philosophy and medicine under the eminent physician Antonio Valsalva. His book "De Sedibus et Causis Morborum" (On the Location and Cause of Diseases) described not less than 640 post mortems in which he tried to locate the disease to a particular organ. He tried to match the clinical symptoms ante mortem with the post mortem changes. Morgagni therefore is generally regarded as the founder of Morbid Anatomy.



**The Anatomy lesson of Dr. Nicholaes Van Tulp (Rembrandt)**

## **Morbid Anatomy – Is it ghoulish tinkering or real science?**

Though the name elicits some degree of fear among some people, including surprisingly some medical doctors, morbid anatomy is a major and inevitable part of the medical science that takes care of Homo sapiens from womb to tomb. It is the study of disease and disease processes using scientific methods. In an effort to look less intimidating in the eyes of the populace, some Departments in Nigeria have changed their names from Morbid Anatomy Department to the Department of Anatomic Pathology. Morbid anatomy is clearly relevant to the practice of clinical and preventive medicine. The preclinical curriculum of anatomy and physiology deals with normal forms (morphology) and functions and the relationship between them. Pathology is the study of abnormal morphology and functions and the relationship between them. The relationship between morphology and function is not always directly proportional. Some patients have severe functional disturbances with only slight morphological changes. Others may have obvious morphological changes but only slight functional disturbances. This discrepancy may be due in part to failure of available techniques to detect subtle structural or functional changes. A small morphological lesion in a critical location may have serious consequences. Conversely, a large lesion in a non critical area may have negligible functional consequences. Changes in morphology are therefore not always directly proportional to changes in function.

With the use of modern technology pathologists can now define morphology at various levels:

1. Gross. This is the description of the appearance of an organ with the naked eye. The extent, dimensions and weight of a lesion may be important. No technologically advanced equipment is needed here.
2. Microscopic. This is the description of a lesion under the microscope. Various models of light microscopes are in use.

3. Immunohistochemical technique is also used by pathologists to demonstrate antigens which are specific for certain tissues. This is widely used in lymphoma diagnosis, in identifying the primary origin of a metastatic tumour, in demonstrating ER/PR receptors or HER-2 status of breast cancer, and in many other areas in diagnostic histopathology. Slides of tissues stained using this method would still have to be examined under the microscope.
4. Ultrastructural. This involves the use of transmission electron microscope to observe sub-cellular changes. This is particularly helpful in the diagnosis of kidney diseases and some tumours arising from the mesenchyme.
5. Molecular pathology. Molecular biology techniques are about the most sophisticated methods in diagnostic histopathology. At the very centre of diagnostic molecular pathology is the amplification of DNA. The Polymerase Chain Reaction (PCR) technique is based on the principle that amplification of a unique target of nucleic acid may be achieved by selecting short PCR primers (oligonucleotides) that flank the DNA of interest. After extraction, the sample DNA is heated to denature (separate) the strands, then cooled to allow the primers to bind to their complementary sequences. The hybridised primers provide a double-stranded template for the heat stable DNA polymerase to synthesise the DNA segment of interest. One PCR cycle consists of three steps:
  - Denaturation
  - Primer annealing and
  - Extension

After 32 cycles of PCR, more than 1 billion identical copies of target DNA are generated. This usually is followed by post amplification processing gel electrophoresis and visualisation with ultraviolet light. Pathologists can use the technique of FISH on fixed, paraffin-embedded tissue biopsies using short fluorescently-labelled DNA or RNA probes to identify specific DNA sequences.

PCR can also be used to amplify an RNA target sequence in a procedure termed reverse transcriptase polymerase chain reaction (RT-PCR). The RNA sequence is first converted to a double-stranded DNA (cDNA) using a reverse transcriptase enzyme borrowed from retrovirus. The cDNA sequence can then be amplified using the standard PCR cycles. RT-PCR is used for detection of RNA viruses, such as HIV and Hepatitis C and also of mRNA of originally large DNA translocations.

FISH provides information on chromosomal gene amplifications, deletions, translocations. For example, amplification of HER-2 oncogene in breast cancer is a prognostic factor in stage II node + breast cancer patients. Determination of HER-2 status therefore is important in determining the suitability of herceptin (trastuzumab) therapy. Dual colour FISH probes usually are used to identify chromosomal rearrangements in human tumours such as the BCR/ABL translocation involved in CML and AML; the IGH/BCL translocation in follicular lymphoma and large cell lymphoma and the IDCH/CCND1 translocation in mantle cell lymphoma.

Because of genetic heterogeneity displayed by tumour cells, the pathologist (i.e. morbid anatomist) is now able to identify the particular cluster of cells of interest and those cells can be extracted for further analysis using laser capture microscopy rather than submitting the entire tissue blocks.

With these and many other molecular techniques in place, the pathologist now has a better understanding of the role of mutation and genetic polymorphism in disease. The next generation of sequencing technologies has already been developed. This is expanding the possibilities to analyse the mutational spectrum of cancer genomes with a comprehensive perspective thanks to their high speed, relatively low cost, and ability to detect all types of genomic alterations.

## **Morbid Anatomy and Diagnostic Histopathology in Ife - where we are presently.**

In the beginning were Odesanmi, Kalidasa and others. When I joined the Department as a Medical Training Fellow in October 1987, there were already three members of staff: Dr W.O. Odesanmi whose promotion to the grade of Professor was announced before the end of that year, Dr. Olusegun Ojo (now Professor Olusegun Ojo) and Dr Simeon Nwosu (now Professor Simeon Nwosu) who actually was a Resident Doctor in Morbid Anatomy at the University Teaching Hospital in Ife at that time. Pathology training in those days was not an easy venture. Resident doctors were very few in the Department as nobody was interested in specialising in "morbid" as they jokingly referred to the specialty. We were seen as mere educated undertakers. However, the profile of morbid anatomists has improved over the years and we faithfully serviced all the clinical departments, dishing out histopathologic diagnoses promptly and efficiently. The autopsy rate was high and most of the cases were hospital autopsies on cases of natural deaths. The rate of hospital autopsies has slightly declined from what it used to be but the converse is the case for coroner's autopsies. Histopathology services have also improved over the years. The number of surgical specimens coming to the Department has increased; cytology services are now available so also is immunohistochemistry.

Immunohistochemistry (IHC) was launched by the current Chief Medical Director Professor Sanya Adejuyigbe under my headship of the Department on the 14<sup>th</sup> of June, 2007. Before then IHC was available only at a private laboratory at the Institute of Medical Research and Training (IMRAT), University College Hospital, Ibadan. The laboratory belonged to Professor Funmi Olopade, an oncologist at the University of Chicago. The director of IMRAT at the time, Professor (Mrs) Falusi was present with her team at the launching of immuno in Ife. So also was Mrs Kemi Eriaghanoma of Gemrook Diagnostics, Canada, an alumna of OAU who gave a seminar and hands on session in immunocytochemistry. To date IHC is thriving at Ife, thanks to the active support of the Chief Medical Director, Professor Adejuyigbe.



There were regular mortality meetings with the Department of Obstetrics and gynaecology particularly during the tenure of Professor Olikoye Ransome-Kuti as the Health Minister who insisted that autopsy must be carried out on every maternal mortality case and the report forwarded to Abuja. We had regular clinico-pathology conference with the Department of Medicine, surgico-pathology conference with the Department of Surgery and morbidity-mortality meeting with the Department of Paediatrics. The academic atmosphere was very vibrant but oftentimes very tense and war-like, with pathologists and clinicians using strong language. That was a prelude to the subtotal collapse of what should otherwise be an avenue for learning, cross-fertilisation of ideas and improvement in healthcare delivery and research. Today, while intradepartmental academic activity is vibrant and thriving, interdepartmental academic activity is a much diminished shadow of its old self. Could this be a matter of self-sufficiency in academic knowledge? Clinicians now hold academic meetings, including morbidity/mortality meetings at the Morbid Anatomy conference hall without inviting the landlords. Let me emphasize here that the pathologist and the surgeon are like Siamese twins that no surgery can separate. They remain partners in progress. The same is true of the relationship of the pathologist with other clinicians. Without the surgeon the pathologist will have no material to work with. Without the pathologist the surgeon will not know what to do with many of his patients. The relationship no doubt is symbiotic.

### **Types of diseases**

Diseases are of different origins and have varying causes. Micro organisms such as bacteria, fungi, viruses are mainly responsible for infectious diseases broadly referred to as inflammatory diseases. Derangement in metabolism can cause metabolic disorders. Congenital diseases are diseases that are present at birth. Derangement in the immune system can lead to immunological disorders. Immunological derangement also underlies many inflammatory diseases. The causes of some diseases are not known but some of the factors that predispose to such diseases are known.

Cancer is in this category of disease. It is important to note that immunological and genetic factors play vital roles in all categories of diseases as they determine the body's response to various insults. The World Health Organisation (WHO) has devised a system of classification of diseases known as ICD (International Classification of Diseases) which already has undergone the 10<sup>th</sup> revision. There is also the International Classification of Cancer in Children (ICCC-0) and many other WHO classifications of cancers of particular organs.

## **Cancer and predisposition**

### **Age**

Some malignant tumours commonly occur in children but are rare in adults. These tumours generally called childhood tumours are uncommon in adults and they include Burkitt lymphoma, some types of rhabdomyosarcoma, acute leukaemias, neuroblastoma, Wilms tumour and others. Some others such as prostate cancer and endometrial cancer are seen in adults. Malignant tumours generally occur more frequently in adults than in children. This may be a reflection of attenuation of immunity with age, accumulation of somatic mutation for decades and some other factors.

### **Genetic factors**

Genetic factors are important in carcinogenesis. Cancer itself is a genetic disorder to the extent that there must be damage to the genome for cells to proliferate and function abnormally. Some cancer syndromes are inherited. Affected individuals have a mutant tumour suppressor gene. An example is the Rb gene. Carriers of mutant Rb gene have a 10,000 fold increased risk of developing retinoblastoma, a malignant tumour of the eye, which often is bilateral. Germline mutation of the p53 gene also results in the Li-Fraumeni syndrome in which an affected individual is prone to developing various types of cancer. Some individuals have rare syndromes characterised by defects in DNA repair that could lead to genomic instability and increased predisposition to cancer. Such syndromes include: ataxia telangiectasia, Fanconi anaemia, Bloom syndrome and xeroderma pigmentosum. Some cancers also have

familial predisposition. An estimated 5-10% of breast cancer cases result from inherited mutations, including those in BRCA-1 and BRCA-2 genes. Individuals with the mutant BRCA-1 or BRCA-2 gene also have one or more first degree relative with breast or ovarian cancer. Although mutation of these genes occurs in no more than 3% of breast cancer patients the genes have made international headlines in recent times because of the identification of one of them by genetic testing in a 37-year old American actress diagnosed with breast cancer. Her mother who died of ovarian cancer at the age of 56 also inherited a BRCA-1 gene. She made the choice of having bilateral mastectomy. BRCA mutations are present in less than 1% of the population. Women with the mutations have 44-78% risk of developing breast cancer by age 70. The BRCA genes are tumour suppressors that are involved in checkpoint functions of the cell cycle related to the progression of the cell cycle to the S phase, particularly by inducing cyclin-dependent kinase inhibitor (CK1) p21. They are thought to promote DNA repair by binding to RAD 51, a molecule that mediates DNA double-strand break repairs, thereby functioning as DNA repair genes.

### **Chemicals, including drugs**

Many chemicals are carcinogenic. Among these are vinyl chloride used in the manufacture of polyvinyl chloride (PVC). It has been associated with a type of liver cancer. Some alkylating and acylating agents, including chemotherapeutic drugs used in the treatment of cancer are also carcinogenic. Some of these, such as chlorambucil, cyclophosphamide and others are direct acting carcinogens that require no metabolic activation to act. They act by damaging the DNA of cancer cells. Unfortunately they can also damage the DNA of normal cells causing oncogenic mutation. Thus while a patient is under treatment for leukaemia, lymphoma or other solid organ cancer with a chemotherapeutic agent, there is a possibility of developing a second malignancy, most commonly acute myeloid leukaemia as a complication resulting in double trouble for the unfortunate patient. Generally, direct-acting carcinogens are weak carcinogens.

Indirect-acting carcinogens require metabolic activation to the ultimate carcinogen and are potent carcinogens. Sometimes they could be metabolised to non carcinogenic products. They include polycyclic and heterocyclic aromatic hydrocarbons, aromatic amines, amides and azo dyes and other groups of chemicals. Chemical carcinogens damage the DNA of cells and particularly target the p53 gene and the RAS gene.

### **Ionising radiation**

Electromagnetic and particulate radiations are carcinogenic. Many of the pioneers in the area of x-ray developed skin cancer. Miners of radioactive elements have a tenfold increased incidence of lung cancer compared to the rest of the population. Survivors of atomic bomb blast at Hiroshima and Nagasaki developed leukemias, mainly chronic myeloid leukemia after a latent period of seven years. Subsequently the incidence of breast cancer, colon cancer, thyroid cancer and lung cancer also increased. The episode of the explosion and fire at the nuclear power plant in Chernobyl, Russia in April 1986 was followed by an epidemic of thyroid cancer especially in children under age 15 years at the time of the accident, some of whom were in utero.

### **Dietary factors**

These are particularly important in cancers of the gastrointestinal tract. Prospective studies involving large populations in various countries have reported that high consumption of red meat and animal fat leads to a higher risk of colorectal cancer than that in persons who eat little or no meat. High intake of refined carbohydrate and low intake of vegetable fibres also predispose to colon cancer.

### **Naturally-occurring carcinogens**

To this group belongs aflatoxin B1 which is produced by the fungus *aspergillus flavus*. The fungi *Aspergillus flavus* and *Aspergillus parasiticus* thrive on grains, peanuts and other foodstuffs under favourable conditions of temperature and

humidity that normally prevail in tropical countries. There is no controversy about the association of aflatoxin B1 with liver cancer (hepatocellular carcinoma). Oyelami and co-researchers have carried out several studies on aflatoxins, particularly as it relates to kwashiorkor and other diseases in children in Ife.

### **Miscellaneous predispositions**

Let us briefly look at other very important but less recognised predispositions to malignancy in our very environment.

- A. Electromagnetic radiation
- B. Formaldehyde
- C. Sodium cacodylate
- D. Diaminobenzidine (DAB)
- E. Paraben
- F. Consumption of charred food
- G. Herbicides and pesticides
- H. The practice of oral sex

### **Electromagnetic fields**

This may be from microwave oven, telecommunication structures, use of mobile phone etc. Non ionising electromagnetic fields are among the fastest-growing forms of environmental pollution with myriads of personal consumer products emitting electromagnetic radiation.

### **Microwaving**

Microwaves are a form of electromagnetic energy that travels at the speed of light. They are used to relay long distance telephone signals, television programmes and computer information across the earth to a satellite in space.

As far back as 1976 the Soviet Union outlawed the use of microwave oven. Microwave oven was originally designed by Nazi Germany for use in their mobile support operation for the invasion of Russia. After a series of research on microwave oven,

the Russians banned its use and also issued international warnings on its hazards to health.

Microwave oven is widely used as a cooking appliance and in the IHC laboratory. While the latter use is innocuous, the use of microwave oven for heating food is associated with health hazards. Microwave cooking is not natural, not healthy and is dangerous to the human body. About 70-80% of families living within this university campus uses microwave for heating food items. The awareness of the health hazards of microwaving is generally very low but seems to be increasing among educated persons. Microwave radiation heats from inside out, unlike normal cooking. Microwaving accelerates structural disintegration of foods and creates cancer-causing agents within milk and cereals. Microwaving also tears apart water molecules forcefully, deforming water molecules in foods (structural isomerism). There is also damage to cell walls and genes by microwaving.

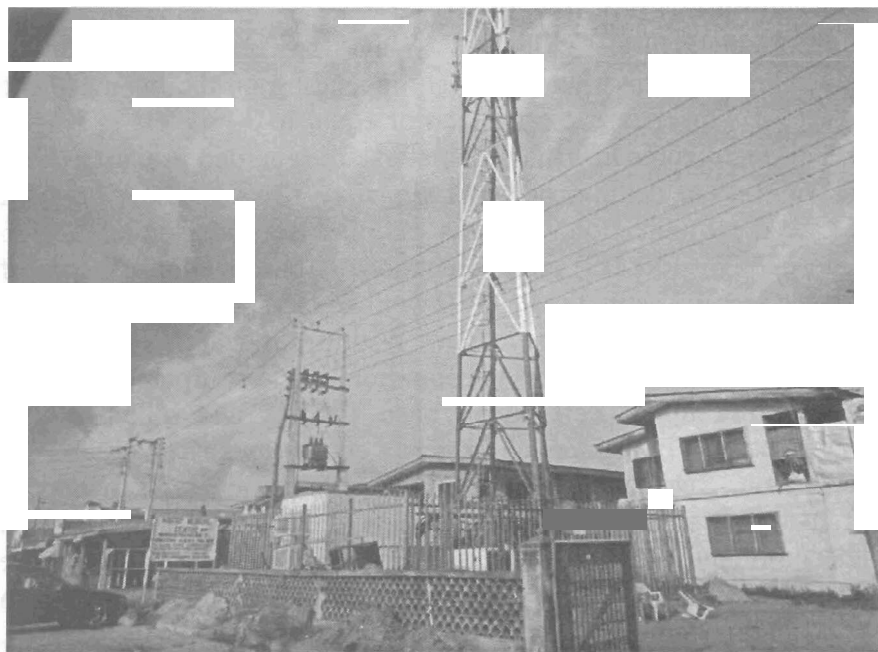
### **Telecommunication structures**

Telecommunication structures may be in the form of telecommunication tower or mast, depending on the height of the structure. Towers are greater than or equal to 30 meters in height, whereas structures less than 30 meters are regarded as masts. They transmit either cellular or wi-Fi signal. Wi-Fi uses Line of Sight (LOS) communication, whereas cellular transmission uses Non Line of Sight (NLOS) communication. A base station consists of three essential structures: a tower erected on a concrete, a generator and a wooden cabin. Within the cabin are: an air conditioner, an inverter and telecommunication equipment.

The setting up of cell phone base stations and other cellular infrastructures in residential areas is a contentious issue in land use regulation. Resistance from nearby residents and land owners is often based on adverse health effects despite reassurances from telecommunications service providers that international exposure standards will be followed. Electromagnetic radiation from telecommunication masts no doubt poses serious health hazards. There are both anecdotal and epidemiological reports of memory

loss, dizziness, sleep disturbances, depression, decreased libido, tremors, increased risk of cancer and leukaemia in populations living close to telecom masts base stations. Even domestic animals are not spared and a whole family could be affected.

What is the situation within the Obafemi Awolowo University campus? There are at least 4 telecommunication towers within the campus. Three of these are found side by side just outside the computer building complex. They are owned by Airtel, MTN and Multilinks telecommunication companies. Another one is located close to the junction of road 9 and road 11. The number of masts is much more than the number of towers. Each bank on campus has its own mast. The computer centre also has its own. The health implication of these towers and masts need to be properly assessed. The building of towers close to residential areas on campus also has to be discouraged.



**A telecommunication tower in front of residential buildings**

## **The use of cell phone**

There's a plethora of opposing information on cell phone health risks. Do they or don't they cause brain tumours and other ailments? Theoretically children are likely to be at a greater risk than adults from developing brain tumours from cell phone use because their nervous systems are still developing and may be more vulnerable to risk factors to cancer. The potential of accumulating many years of cell phone use is also there. However, some studies did not find any association between cell phone use and brain tumour in children. Takabayashi et al (2008) in Japan observed no consistent increase in the overall risk of meningioma and glioma among mobile phone users. There was also no increasing trend in risk in relation to cumulative length of use or cumulative call time. The weight of the current scientific evidence has not conclusively linked cell phone use with any adverse health problem, but more research is needed.

## **Formaldehyde**

Formaldehyde (methylene oxide) is an industrial organic chemical with a pungent odour. It is the simplest aldehyde with a formula of  $\text{CH}_2\text{O}$ . In the industry it is used in the manufacture of building materials and household products. Thus, it may be present in substantial concentrations both outdoors and indoors. It is widely used in the histopathology laboratory. It is an essential reagent used in the preservation of surgical tissue specimens and for preservation of cadavers. Unconfirmed reports also insinuate that some concentration of formalin is used for the preservation of imported chickens and turkeys. Exposure to formaldehyde may cause watery eyes, burning sensation in the eyes and nose and can make an individual cough or wheeze and trigger asthmatic attack. Formaldehyde is known to be a human carcinogen based on evidence on carcinogenicity from studies in humans. It was listed as "reasonably anticipated to be a human carcinogen" from studies in experimental animals as far back as 1981. Additional studies in humans over the years have confirmed formaldehyde to be a human carcinogen.



Exposure to formaldehyde is associated with increased risk of developing nasopharyngeal cancer, sinonasal cancer and lymphohaematopoietic cancers, notably myeloid leukaemias. The level of exposure and the duration are important. Mask should be worn when working with formaldehyde-containing chemicals in the laboratory. The use of fume chambers, where available is also recommended.

### **Sodium cacodylate**

Sodium cacodylate is a poisonous arsenic-containing salt formerly used in the treatment of skin diseases and leukaemia. It is used as a buffer in the preparation and fixation of tissue specimens for processing for electron microscopy in the histopathology laboratory. It is highly toxic by ingestion, inhalation or skin contact. It is genotoxic in humans, causing apoptosis and shorter DNA strands. It is weakly carcinogenic but acts as a strong tumour promoter in the liver and kidney.

### **Diaminobenzidine (DAB)**

DAB is a chromogen widely used in the form of tablet in the indirect immunoperoxidase technique in the histopathology laboratory. All benzidine derivatives are considered carcinogenic. DAB has been found to be mutagenic. DAB must be disposed off with caution after use. Gloves must be worn when handling DAB in the laboratory. In pathology laboratories in the developed nations DAB and other carcinogenic chemicals are usually disposed of in a separate waste bin. Detoxification of DAB after use involves oxidation by potassium permanganate and sulphuric acid.

### **Paraben**

It is advisable to look at the various ingredients in a deodorant or body cream at the point of purchase. Parabens (methylparaben, propylparaben etc) are esters of para-hydroxyl benzoic acid. Paraben is a widely-used antimicrobial preservative in the cosmetic industry because of its bactericidal and fungicidal properties. However, there are lots of controversies on the use of parabens.

Whereas it is not very certain whether parabens are carcinogenic they have been found in breast cancer and they have the ability to slightly mimic oestrogen, a steroid hormone known to play a role in the development of breast cancer. Aside from the controversy on the carcinogenicity of parabens, studies have shown that methylparaben applied on the skin may react with ultraviolet light to induce DNA damage and increase skin ageing. This observation is very important to people living in the tropical environment.

### **Consumption of charred food**

More than two centuries ago, Sir Percival Pott, a British surgeon correctly attributed scrotal skin cancer in chimney sweeps to chronic exposure to soot. Roasted corn and roasted plantain are commonly consumed in Nigeria. In the process of roasting, these food items, corn in particular, are often badly burnt. As a result a large percentage of hydrocarbon is consumed together with the food. The contribution of this to the burden of cancer of the gastrointestinal tract or other sites in Nigeria is not known.

### **Herbicides and pesticides**

Herbicides, pesticides, insecticides and fungicides are various chemical agents that are widely used in agriculture. Nematocides are no longer in use because of their serious adverse effects. Carbofuran has also been banned and withdrawn from the market because of adverse effects. Fungicides are popularly used by cocoa farmers in the Ife-Ijesa area of Osun state. Pesticides have both human health and environmental health risks. Some pesticides are extremely toxic for both human beings and the environment and can lead to hormone irregularities or cancer. Pesticides and herbicides used in both agricultural and home appliances seep into the ground surface and eventually reach the groundwater. In Ile-Ife, outside of the university campus, an estimated 70-80% of the population depend on groundwater for daily usage. The percentage is higher in rural settings in Nigeria. In the highbrow Parakin area of Ile-Ife, for example, there are just about two or three functional boreholes serving the whole area.

Pesticides have carcinogenic effects and children are more vulnerable to the carcinogenic effects than adults when exposed to high levels in food, in drinking water and from inhalation. Unfortunately no impact assessment study on humans and the environment has been conducted in Ife. Dr. Samson Deji recently conducted a study on the awareness of pesticide residues in locally available food and condiments among food sellers in Ife area. The study showed most of the food sellers use phostozin, an organophosphate compound as preservative for cereals (rice, bean, maize) in Ile-Ife area. Majority of those aware of the health hazards are literate school leavers. They are the ones likely to exercise caution in the use of the pesticide. Cereals must be thoroughly washed with water before cooking.

### **Oral sex and nasopharyngeal cancer**

The rise in the incidence of nasopharyngeal cancer in recent times has been blamed on oral sex. Oral sex may cause more cases of throat cancer in men than smoking and there are findings that strongly suggest that the human papilloma virus may play a major role in the carcinogenesis of urogenital and nasopharyngeal tumours. Huang and Seow in Taiwan reported the link of nasopharyngeal cancer with the practice of orogenital sex in husbands of two patients with cervical cancer. Human papilloma virus DNA was detected in the cervical cancers and the nasopharyngeal carcinomas of their husbands using the polymerase chain reaction. Both husbands are non smokers.

### **Aetiology and Pathogenesis of lymphomas**

My major contribution to knowledge is in the area of lymphoreticular pathology. This encompasses lymphoid malignancies (lymphomas) and reactive lymphadenopathies. Lymphoreticular pathology and haematopathology are interconnected.

Lymph nodes are part of the secondary or peripheral lymphoid organs which also include the spleen and Peyer's patches. They are sites where lymphocytes encounter antigens and undergo antigen-

driven proliferation and differentiation. Adaptive immune response to lymph-borne protein antigens are initiated in lymph nodes. Tertiary lymphoid organs which are acquired lymphoid tissues in the stomach, the skin, respiratory and reproductive tracts in response to infection are also important sites of lymphoma.

Lymphomas are tumours of the lympho-haematopoietic system and they are classified into two broad categories: Hodgkin lymphoma (HL) and other lymphomas, which, for lack of a better terminology are generally referred to as non-Hodgkin lymphoma (NHL), depending on the presence or absence of the Hodgkin Reed-Sternberg (H-RS) giant cell.

HL was first described by an English physician Thomas Hodgkin in 1832. Thomas Hodgkin was the father of preventive medicine and one of the most prominent pathologists of his time. He studied at Guy's Medical school (now part of King's College, London) and University of Edinburgh, Scotland. He later travelled to France where he learned to work with the stethoscope, a recent invention of Rene Laennec at that time. Failing to get a consultant appointment at Guy's Hospital he turned to philanthropic work. In 1866 he accompanied his close friend Sir Moses Montefiore to Palestine where he contracted dysentery. He died in April 1866 and was buried at Jaffa.

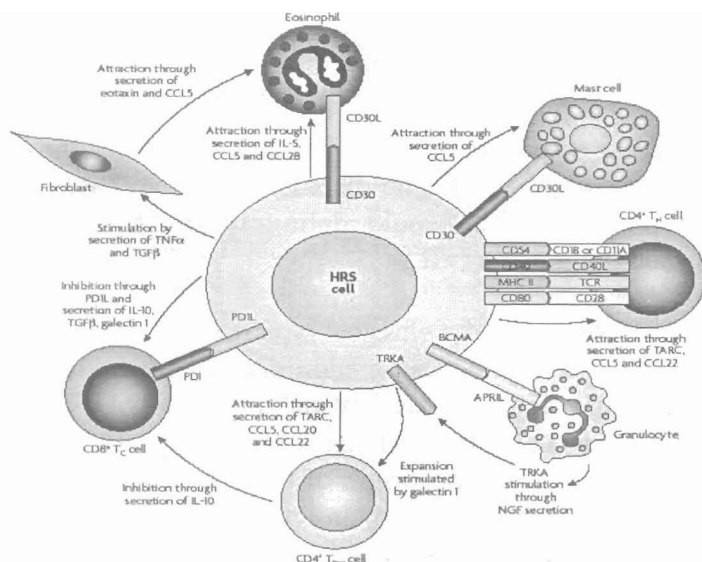
A review of Hodgkin's original 7 cases revealed they were unlikely to be comprised of one disease. Only two cases showed microscopic features that would definitely fit the present day criteria for the diagnosis of HL.

HL in 95% of cases is of the classical type (cHL). The rest belongs to the nodular lymphocyte predominance Hodgkin disease (NLPHL) subtype characterised by the presence of lymphocyte predominance (LP) cells, formerly called popcorn cells. The clonal nature and the B-lymphocyte origin of both the H-RS cell and the LP cell were established in 1994. In spite of its B-cell origin, B-cell markers such as CD20 and CD79a are down-regulated in H-

RS cell, though PAX-5 may be weakly expressed. LP cells, on the other hand consistently express CD20 and Bcl-6, a hallmark of germinal center B-lymphocyte.

There had been years of controversy surrounding the nature of the H-RS cell. The malignant nature of the cell has become obvious from the clonal rearrangement of the IgV genes, and very rarely TCR gene rearrangement. H-RS cell clones are almost always composed of mixtures of mononuclear Hodgkin and multinuclear Reed-Sternberg cells. Cell fusion does not play a role in the generation of the Reed-Sternberg cells rather, they derive from Hodgkin cells through a process resembling endomitosis, i.e. nuclear division without cellular division. Hodgkin cells of HL cell lines give rise to new mixture of H-RS cells, but Reed-Sternberg cells are generally unable to undergo further proliferation.

The microenvironment surrounding H-RS cell is unique and is a determinant of the initiation and progression of HL. The H-RS cell orchestrates the infiltration and activation of multiple cells types into the lymphoma microenvironment through the secretion of cytokines and chemokines. Eosinophils may stimulate interaction of CD30-CD30L. Granulocytes stimulate H-RS cell through



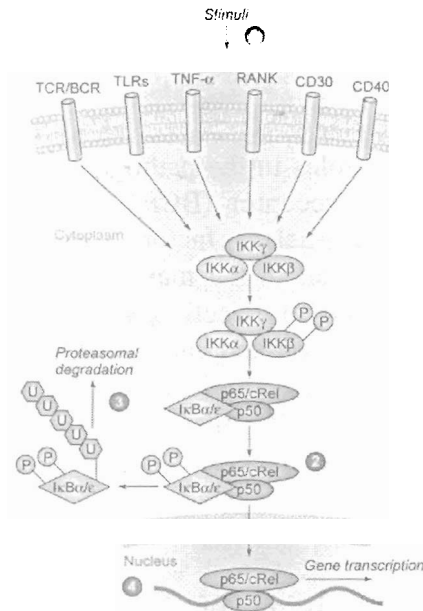
APRIL-BCMA interaction. Cytotoxic T-cells and NK cells are inhibited through Treg cells by secretion of IL-10. Fibroblasts are attracted by secretion of TGF- $\beta$  and TNF- $\alpha$ .

Several signalling pathways play vital roles in the pathogenesis of lymphomas. These include the B-cell receptor (BCR) pathway, Notch-1 signalling pathway and the nuclear factor Kappa B (NFkB) signalling. Notch - 1 is important in the maintenance of haematopoietic stem cell and inhibition of B-cell development. Notch -1 activation leads to pro-proliferation and anti-apoptosis in H-RS cells. Activation of Notch -I is mediated by its ligand Jagged -I, which is expressed by cells in the HL microenvironment. Incidentally, H-RS cells have down regulated the Notch - I inhibitor Deltex.

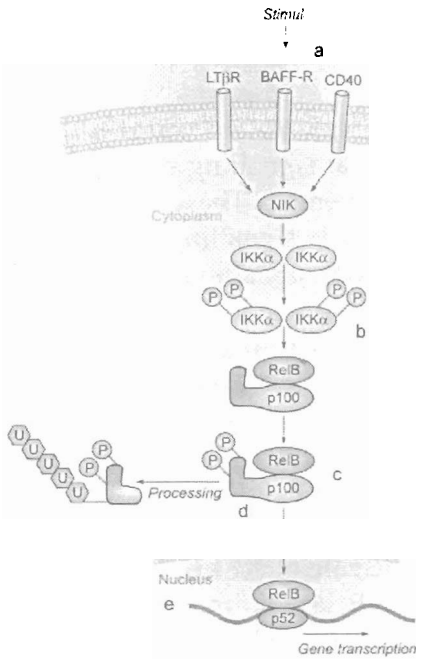
### **The role of NFkB**

NFkB is a transcription factor consisting of five proteins physiologically kept inactive by association with inhibitor proteins IKB alpha etc. NFkB regulates the pro-proliferative and anti-apoptotic gene expression programmes in lymphocytes. NFkB is the effector of transforming events in HL causing uncontrolled stimulatory signalling. NFkB is activated by both the canonical (classical) and the non-canonical (alternative) signalling pathways. Both pathways lead to the phosphorylation of IKB by IKB kinase (IKK). This induces IKB polyubiquitination and degradation by the ubiquitin-proteasome pathway. NFkB dimmers are subsequently released, translocate to the nucleus and initiate transcription.

### A) Activation of the Canonical NF- $\kappa$ B Pathway



### B) Activation of the Alternative NF- $\kappa$ B Pathway

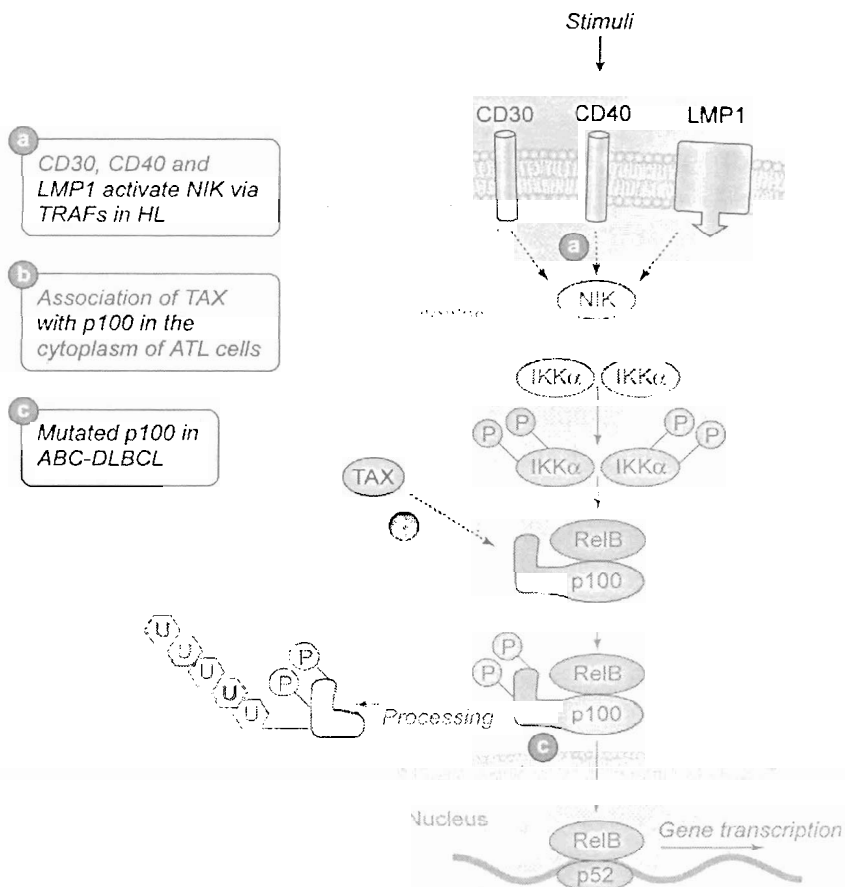


Source: [bloodjournal.haematologylibrary.org](http://bloodjournal.haematologylibrary.org)

The canonical pathway is activated by pro-inflammatory cytokines such as Interleukin-1 (IL-1) and tumour necrosis factor (TNF), pathogen-associated molecular pattern (PAMP), T-cell receptor (TCR), B-cell receptor signalling etc.

Alternative pathway signalling cascade is activated by CD40, lymphotoxin beta receptor, BAFF receptor.

## Aberrant Activation of the Alternative Pathway



**Source: [bloodjournal.haematologylibrary.org](http://bloodjournal.haematologylibrary.org)**

Epstein-Barr virus (EBV) LMP-1 acts as a constitutively active CD40R and aberrantly (i.e. ligand-independently) activates the NFκB, AP1 and JAK/STAT signalling pathways to promote B-cell survival and proliferation. EBNA-2 another EBV gene encodes a nuclear protein that mimics a constitutively active Notch receptor. Both classical (canonical) and the alternative pathways are activated by LMP-1 inducing up-regulation of cytokines, chemokines and anti-apoptotic proteins.



Factors implicated in the aetiology of HL are largely environmental (viral infection) and genetic. The risk of concordance for HL in monozygotic twins is 100, compared to dizygotic twins with no increased risk. Viruses are linked to about 20% of malignancies worldwide. Retroviruses account for 8-10% of the viruses.

### **The role of EBV**

EBV is a herpes virus with a worldwide distribution. Over 90% of healthy adults are persistently infected by this virus with a reservoir of infection in memory B-cells. The three most important EBV-associated lymphomas are Burkitt lymphoma, Hodgkin lymphoma and lymphoma occurring in the context of immune suppression. The risk of developing HL is up to three times higher in those with a history of infectious mononucleosis and patients with HL have a high antibody titre to EBV at diagnosis and years before the disease onset. Lytic infection by EBV is associated with production of viral particles and death of the infected cell. In latent infection, which is associated with transformation by EBV, only a restricted group of viral antigens is expressed. The expression pattern of EBV-encoded genes (LMP-1, LMP-2, EBNA-1) is characteristic of latent viral infection.

The search for the aetiology of NHL is partially successful. Congenital and acquired immunodeficiency states are the best recognised risk factors for developing NHL. HIV has been blamed for the increase in the incidence of NHL. However, the increase in the incidence of lymphomas had begun before the AIDS pandemic in the 1980s and the contributions of HIV/AIDS to the total number of lymphoma diagnosed in developed countries remain small. Other viruses associated with NHL are EBV, Human T-cell Leukaemia Virus (HTLV) and Human Herpes Virus type 8 (HHV-8) otherwise known as Kaposi sarcoma-associated herpes virus (KSHV). HHV-8 is associated with multicentric Castleman disease, Kaposi sarcoma and primary effusion lymphoma (PEL), a rare form of lymphoma that occurs in body cavities. PEL is seen in HIV-positive patients with low CD4 cell counts.

## **Other Associations**

There are documented links between autoimmune-based chronic inflammation and lymphoma, for example, the association of Hashimoto thyroiditis and thyroid lymphoma; the association of Sjogren syndrome with salivary gland lymphoma. There are also consistent associations between rheumatoid arthritis and systemic lupus erythematosus (SLE) with both marginal zone lymphoma and diffuse large B-cell lymphoma (DLBCL). Immunodeficiency states such as Chediak-Higashi syndrome and X-linked lymphoproliferative disease (Duncan syndrome) predispose to lymphoma. The association between *Helicobacter pylori* and gastric marginal zone lymphoma (MZL) is well known.

## **Exposure to petrochemicals**

Exposure to benzene, an industrial chemical and component of gasoline (petrol), diesel fuels as well as paints, glue, tobacco smoke is a widely recognised cause of leukaemia. There is a statistically significant association between NHL risk and probable benzene exposure. A number of studies in mice have confirmed this association. There are documented reports of increase in the incidence of lymphoma among tanker crews and automobile mechanics in the United States. This has serious implications in a country like Nigeria where the practice of siphoning petrol by auto mechanics is prevalent. Benzene is similar to alkylating drugs and radiation in producing leukaemia. It is plausible that it might also produce lymphoma by similar mechanisms.

The aetiology of the majority of NHL however, remains unknown. Excessive exposure to electromagnetic fields is thought to play a role. Attention is also being focused on the role of herbicides and pesticides. Contamination of ground surface water by nitrites from fertilisers, hepatitis C virus infection as well as occupational exposure to some solvents used in hairdressing may play a role in the development of lymphoma.

## **Viral origin of T-cell lymphomas**

### **Herpes Viruses**

EBV is associated with nasal type NK/T cell lymphomas. This is seen mainly in Asia and it affects gut-associated lymphoid tissues, nasal cavity, lungs and the Waldeyer's ring. EBV is also associated with primary cutaneous CD40+ anaplastic large cell lymphoma (rare). Human herpes virus type 8 (HHV-8) is associated with T-cell primary effusion lymphoma (PEL).

### **Retroviruses**

Human retroviruses are more commonly implicated in T-cell malignancies than herpes viruses.

#### **HTLV-1**

This is associated with adult T-cell leukaemia/lymphoma.

HTLV regulatory factors include:

- pTax (p40), a transactivator that activates the transcription of both viral and cellular genes involved in T-lymphocyte growth and proliferation. Tax activates the NFkB pathway. In contrast to transient NFkB activation in response to cytokines, activation by tax leads to constitutive nuclear levels of NFkB.
- Tax transactivates cellular promoters including those of cytokines (IL-13, IL-15), cytokine receptors (IL-2R alpha) and co-stimulatory cytokine receptors (OX40/OX40L) leading to activation of signalling cascades (e.g. JAK/STAT, P13 kinase etc). Tax also binds to CDK holoenzymes and/or inactivating tumour suppressors (p53, DLG) to promote growth.
- Tax silences cellular checkpoints, which guard against DNA structural damage and chromosomal missegregation.
- Induction of IL-2 and IL-2R
- Suppression of release of E2F-DP-1 complex from pRb to the nucleus.
- Combines with cyclin B-related protein to induce polyploidy.

## HIV-1

- Human immunodeficiency virus is another retrovirus that is associated with malignancy. Lymphoma is a late event in HIV infection. The current risk factors for lymphoma in HIV/AIDS patients are: high viral load, advanced age (> 35years) and male gender. Highly active anti-retroviral therapy (HAART) has led to a decrease in the incidence of Kaposi sarcoma in HIV+ patients; the reduction in the incidence of NHL is small or non-existent. AIDS patients are now living longer and sustaining fewer opportunistic infections and malignancy is becoming increasingly prominent as a cause of death.

Finally, it is important to know that most cases of HL and NHL occur in people who do not have identifiable risk factors, and most people with identifiable risk factors do not develop HL or NHL.

## **Contribution to Knowledge**

### **Lymphoreticular pathology and Haematopathology**

My major contribution to knowledge is in lymphoreticular pathology, a major part of haematopathology, as earlier mentioned. Very few pathologists have shown interest in this area until very recently. This is not unconnected with the fact that benign lymph node proliferations have many appearances under the microscope and may sometimes be difficult to differentiate from malignant proliferations without the use of specialised techniques, which in most laboratories are not available till today. Malignant proliferations also may not be easy to characterise using only routine stains.

The lymph node and the lymphoreticular system play a major role in innate and adaptive immune responses. Peripheral lymphadenopathy may be secondary to a benign disease outside of the lymph node (reactive lymphadenopathies), it may be as a result of lymphoma or may be due to a malignant tumour spreading out of the primary location to the lymph node, (metastatic cancer).

Acute lymphadenitis poses little diagnostic problem as the cause is usually apparent. For example, inguinal lymph node enlargement (referred to as 'petele' by the Yoruba) is mostly due to infection on the feet which is apparent on examination. Persistent peripheral lymphadenopathy not associated with malignancy or focal lesion, on the other hand poses a difficult diagnostic problem. Our researches showed that most of the patients with peripheral lymphadenopathy (49.3%) had tuberculosis. Why the majority of those with tuberculosis were girls remain unexplained. From our larger study of 944 cases which included bone marrow trephine biopsies and spleen, non-Hodgkin lymphoma and tuberculosis accounted for the highest percentages of lesions seen in lymph nodes and extranodal lymphoid tissues. Patients with chronic lymphocytic leukaemia showed a significantly higher mean age than those with non-Hodgkin lymphoma. The preferred destinations for metastasis of malignant tumours were cervical and axillary nodes. It is not surprising that most of these cases were from breast cancer patients. Non-Hodgkin lymphoma and reactive changes were the most commonly encountered pathologies in the bone marrow. Histopathology studies on the bone marrow are rare in Nigeria, presumably due to lack of bone marrow trephine biopsy materials to work with by pathologists in many centers. This is not so at the Teaching Hospital in Ife; the Department of Haematology and Immunology constantly provides the opportunity of reporting on marrow trephines. The Departments of Haematology and Immunology and Morbid Anatomy and Forensic Medicine have made giant strides in the advancement of haematopathology in Nigeria. On a visit to Ife in 2010 to launch telepathology, the Director of pathology education at the International Network for Cancer Treatment and Research (INCTR) Professor Nina Hurwitz remarked that the OAUTHC is one of the very few tertiary health institutions in sub-Saharan Africa where bone marrow trephine biopsy is routinely performed. It is interesting to know that Professor Hurwitz and her visiting colleagues are familiar with most countries in Africa and other continents. I was subsequently invited to visit the Institute of Pathology in Basel, Switzerland in May, 2011 for update on bone marrow pathology.

Our study on the spleen, as expected was exclusively on splenectomy samples mostly from victims of road accident who survived and those with haematological malignancies. Most of the spleens showed lacerations and haemorrhage from road traffic accident. Other indications for splenectomy in Ife-Ijesa area from our study included chronic lymphocytic leukaemia, hypersplenism of unknown origin, lymphoma, sickle cell anaemia, essential thrombocythaemia etc. The spleen plays a major role in immunity. Removal of the spleen, known as splenectomy, has serious consequences on the body. The critical role of the spleen in preventing infection is well known. As an immunologic organ the spleen participates both in innate and adaptive immune responses and is an important site for haematopoiesis in foetal life. Postsplenectomy infections are usually due to encapsulated bacteria, including *Streptococcus pneumoniae*, *Haemophilus influenzae* type b and *Neisseria meningitides*. Overwhelming sepsis is the most dreaded complication of the postsplenectomy state. What lessons we can learn from all these? When traumatic damage necessitates splenectomy, attempts should be made at splenic preservation by the surgeon. Accessory spleen and partial splenectomy allow retention of the immunologic function of the spleen. Strategies geared towards reducing road traffic accident should also be enforced.

## Lymphoma

Lymphomas are tumours of the immune system. Worldwide, most are of B-lymphocyte origin. The diagnosis and classification of lymphomas are aided by IHC. IHC is also very important in the differential diagnosis of benign and malignant lymphoproliferation where they constitute a diagnostic conundrum. It is possible, in many cases to distinguish Hodgkin from non-Hodgkin lymphoma based on Haematoxylin and Eosin (H&E) stain only. Some subtypes of non-Hodgkin lymphoma such as follicular lymphoma grades 1 and 2 can also be diagnosed on H&E stain only. However, without IHC, and also ISH, the pathogenesis and the molecular signature of the disease are obscured. This also has implication for treatment and prognosis. At the time I joined the department, late

in 1987, our diagnosis of lymphoma was based on the Rappaport classification, which is based on H&E stain only, although at that time Lukes and Collins had already devised a new classification based on the fact that the lymphocyte is not just a static end point but consists of two different entities: the B-lymphocyte and the T-lymphocyte. This knowledge was as a result of advancement in immunology. It later became obvious with the use of cell markers that, most of the entities diagnosed as histiocytic lymphoma using the Rappaport classification did not originate from histiocyte, some in fact were T-cell tumours. Histiocytic lymphomas are not as common as previously believed before the advent of IHC. The Rappaport classification, devised by Dr Henry Rappaport was based on light microscopic appearance of H&E-stained sections without the use of cell markers. We later abandoned the Rappaport classification and switched to the Working formulation, still using H&E stain only in the Department. This was a time lymphoma classifications were proliferating faster than rabbits to warrant a letter to the Lancet magazine suggesting a classification of classifications. Everyone was confused, including the surgeons who admonished the pathologists to put their house in order or they too would be compelled to devise their own classification for pathologists. The great English writer Charles Dickens probably foreshadowed this scenario in haematopathology in *A Tale of Two Cities* when he wrote: "It was the best of times, it was the worst of times, it was the age of wisdom, it was the age of foolishness..." To some lymphomaniacs, or should we say, lymphologists, the Working Formulation was dead on arrival. Nevertheless, the classification persisted for a while. Driving these continual reclassifications are:

- A). New data on the biology of lymphoma.
- B). Uncertainty as to what is important in the accurate classification of lymphomas (is it morphology, immunophenotype, genotype, clinical behaviour or some other things?).
- C). Advances in immunology.

I dare say we have not seen the end of classification of lymphomas as advancement in immunology and molecular genetics continue. It should be noted that HL is predominantly a nodal disease, unlike NHL. HL also has a predetermined mode of spread, from one lymph node or chain of nodes to anatomically contiguous lymph nodes, unlike NHL which has a haphazard mode of spread. NHL, unlike HL may have a leukaemic phase, when the lymphoma cells spill over into the bloodstream, leading to leukaemia. Leukaemic phase is particularly common with the low grade lymphomas. NHL therefore is generally a more biologically malignant disease than HL.

My research into lymphoma showed that NHL predominated over HL and that the occurrence of NHL is twice more common in males than in females. The intermediate grade lymphomas are the most common types seen in adults outside the paediatric age group. There is the possibility of cure for this category of lymphoma, and this underscores the significance of early diagnosis and treatment. Unfortunately patients present to the hospital late. Many of them cannot afford the cost of full investigation and abscond midway into the investigation. Many cannot afford the cost of treatment and simply fail to turn up at the clinic. Fake addresses given by patients also militate against follow-up. In such circumstances efficacy of treatment and mortality data are difficult to evaluate. Prognostic histopathologic markers of lymphoid malignancies are also difficult to determine and the result is to rely on data on Caucasians.

The first study to unravel the possible pathogenesis of Hodgkin lymphoma in Nigeria was undertaken by us (Adelusola K.A., Titiloye N.A. et al). Using the indirect immunoperoxidase technique we determined the role of Epstein-Barr virus latent membrane protein-1 in the pathogenesis of Hodgkin lymphoma. Our research confirmed our earlier finding that the mixed cellularity subtype of classical Hodgkin lymphoma predominates in Nigeria. Beyond that we were able to establish that EBV plays a role in 60% of cases of Hodgkin lymphoma in Ife-Ijesa area of Osun State, raising the possibility of the activation of the



alternative pathway and to some extent also the canonical pathway in the pathogenesis of Hodgkin lymphoma in our environment. Incidentally EBV positivity is associated only with the mixed cellularity subtype in our study. Our research also showed that cervical lymphadenopathy and splenomegaly were the two most common presenting symptoms in patients with Hodgkin lymphoma. This study further shows the pivotal role of IHC in the diagnosis of lymphoma as three of the cases originally diagnosed as Hodgkin lymphoma by H&E only turned out to be non-Hodgkin lymphoma with IHC. These were 2 cases of diffuse large B-cell lymphoma and a case of anaplastic large cell lymphoma (ALCL). Incidentally, ALCL is a differential diagnosis of CD30 + lymphomas.

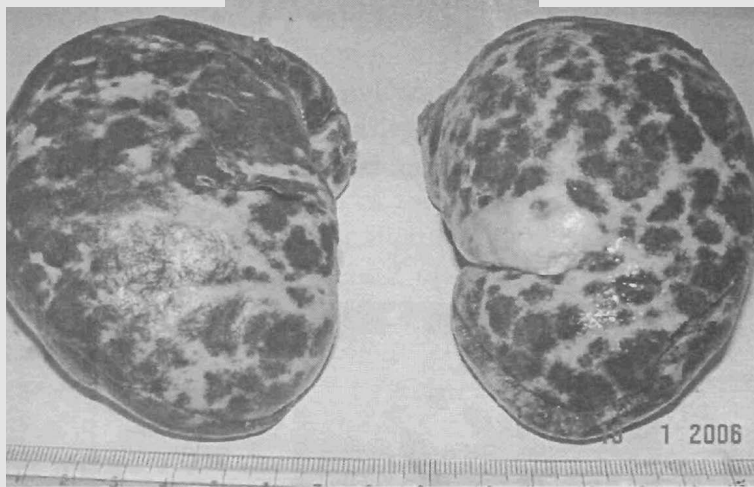
### **Follicular lymphoma**

Follicular lymphoma (FL) is the second most common lymphoma in Caucasians, after DLBCL. It is an indolent but incurable type of non-Hodgkin lymphoma. It is generally accepted that FL is uncommon in blacks. The question is, are we missing the diagnosis? Are we seeing FL at late stages, like stage III and stage IV when the follicular architecture has disappeared? Studies in Africans, including our own in Ife, have shown that FL is not as common as other types of lymphoma. A case of FL with monocytoid B-cell from our center was presented at a conference on lymphoma in Africa at Institut Curie, Paris, in May 2011. Unlike most FLs this particular case was Bcl-2 negative. Why FL is rarely seen in blacks cannot be explained. Recently the sub-Saharan Africa Lymphoma Consortium (SSALC) headed by Professor Leona Ayers of the Ohio State University attempted to study AIDS and lymphoma in Africa. Professor M.A. Durosinmi and I are collaborators representing OAU in that project. Despite the use of IHC, in-situ hybridisation and other sophisticated technique no case of FL was identified in our samples. However, a study conducted in Zaria also by SSALC showed that 16% of their cases (6 out of 42) were FL. Lymphomas in Ife have recently been characterised using Tissue Microarray Analysis. The results however, are yet to be published.

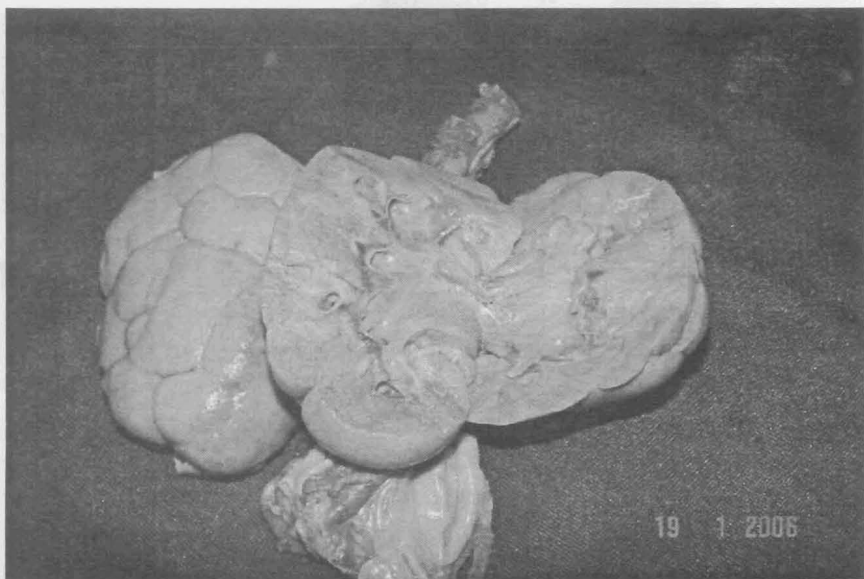
We also studied lymphomas at specific extranodal sites such as the testis (Omoniyi-Esan, Adelusola et al) and the kidney (Olowu, Adelusola et al). Testicular tumours generally are uncommon in blacks. Most cases encountered in Ife are paratesticular rhabdomyosarcoma. Testicular lymphoma is also not common but is known to be aggressive and in our report most are of diffuse large cell variant, and is bilateral in one of the cases we reported.



**Burkitt Lymphoma in a child**



**Renal involvement with a non-Hodgkin lymphoma in a child. The kidneys are enlarged and haemorrhagic.**



**Another pattern of renal involvement with non-Hodgkin lymphoma. The kidneys are bilaterally lobular.**

## Oncology

Oncology is the study of tumours. The medical term for tumour is neoplasm. The best definition of tumour, so far is offered by the eminent British oncologist Sir Rupert Willis: A neoplasm is an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissues and persists in the same excessive manner after cessation of the stimuli that evoked its change. Affliction of man by tumours is not new. King Jehoram of Judah because of his wickedness and idolatrous practices was afflicted by an incurable disease in the bowels (2<sup>nd</sup> Chronicles 21: 15, 18). That incurable disease most likely was colon cancer.

Until recently, the subject of neoplasia in African children had received little or no attention for decades. It is now known that there is considerable variation in the pattern of childhood malignancies worldwide. There is a high incidence of lymphoma and a low incidence of leukaemia in developing countries of Africa. In Europe and North America the reverse is the case. In collaboration with other researchers, I studied 157 malignant solid tumours in children at OAUTHC. We established that lymphomas formed the bulk of the tumours seen in children with a vulnerable age at between 6 and 13 years. Alveolar rhabdomyosarcoma, a malignant tumour occurred only in boys. Alveolar rhabdomyosarcoma is notorious for its poor prognosis. Surprisingly while rhabdomyosarcoma is not common in Kenyan children the embryonal and the botryoid variants are the ones most common in American children. Girls were more afflicted by osteogenic sarcoma and nephroblastoma. Surprisingly no brain tumour was recorded in our study. This is similar to reports from Zaria and Calabar but at variance with findings from studies in Lagos and some other centers in Nigeria. Astrocytoma, oligodendroglioma, medulloblastoma and other brain tumours have been reported from the various centers.

Breast cancer, a malignant tumour is one of the most common causes of cancer deaths in females. In Nigeria it is often associated with a poor prognosis for a number of reasons. The male also has

rudimentary breasts which could rarely be affected by cancer. We did a histopathologic characterisation of breast cancer both in the female and in the male. Our researches on female breast cancer showed an increasing incidence in the number of cases seen at the hospital, probably as a result of increase in the awareness of the disease. Women aged 40-49 years accounted for the bulk of the cases. The peak age incidence for the disease in Caucasians is a decade later than in Africans. Women aged 60-69 years also show a higher incidence than previously reported. The infiltrating ductal carcinoma, Not Otherwise Specified (NOS) was the most common histopathological type. Medullary and papillary variants were next in frequency. Medullary carcinoma has a very good prognosis. In a study of 212 breast cancer patients by Adesunkanmi et al we observed that 74% of the patients had advanced disease (stages 3 and 4) at diagnosis, 79.2% had pregnancy early in life and were multiparous. It thus seems that the risk factors for breast cancer in blacks may slightly differ from the risk factors in Caucasians.

Our study on the cancer of the male breast confirms the universal assertion that it is indeed rare. We encountered only 10 cases out of 513 cases seen in over 19 years of the existence of the Teaching Hospital. There seems to be familiar predisposition in at least two of those cases. The first was a 60-year old man who claimed his mother had died of breast cancer. The second was a 41-year old manager who claimed that four members of his family died of breast cancer at relatively young ages. Members of families like these should be strongly advised to go for genetic testing for breast cancer susceptibility genes in order to prevent future disaster.

## **Nephropathology**

My involvement in nephropathology is partly through collaborative study with Professor Olowu a paediatric nephrologist. Again, OAUTHC is one of the very few Teaching Hospitals in Nigeria where renal biopsies are commonly performed on patients with kidney diseases. The reason for this is hard to fathom but speculations abound. Our collaborative research established that most of the causes of acute renal failure in children

in Southwestern Nigeria are preventable and that most of the patients present with oliguric acute renal failure. Plasmodium falciparum malaria still accounts for a large percentage of acute renal failure of secondary aetiology. We also reported two cases of Burkitt lymphoma of the kidneys with an unusual presentation as acute renal failure. The lesson we learned from this is that Burkitt lymphoma should be suspected in a child with rapidly enlarging kidneys and acute renal failure. Professor A. Akinsola, the eminent physician has contributed tremendously towards the development of nephrology in Ife and in Nigeria.. Resident doctors trained in Ife have the rare privilege of understanding the art and science of reporting not only routine renal biopsy specimens but also renal transplant biopsies. This has been made possible through the vision of Professor A. Akinsola and his highly capable and dedicated team in establishing OAUTHC as the first tertiary institution to carry out renal transplant in Nigeria, an operation performed by a Nigerian surgeon Dr. T.A. Badmus of OAU. Unfortunately this landmark event received very poor media coverage. The OAUTHC under the leadership of Professor D.O. Akinola, the immediate past Chief Medical Director was magnanimous in sending me to Manchester Royal Infirmary in 1998 to train in renal allograft rejection pathology under the eminent nephropathologist Professor Ian Roberts. To date, the Ife renal transplant programme is on course and thriving. I have been responsible for reporting renal biopsies, including renal transplant biopsies in the Department of Morbid Anatomy, OAUTHC for many years. This is in addition to assisting or supervising resident doctors in morbid anatomy and in nephrology unit with their Part II Final examination projects.

### **Autopsy pathology**

From necromancy to witchcraft and other occult practices, man has always sought for the knowledge of the truth from among the dead, either by summoning their spirit or raising them bodily. King Saul was no exception. His infamous visit to Endor was to consult a familiar spirit in order to know the truth about his ineluctable fate from Samuel, who was already dead. The search for the truth among the dead continues till today both in the occult and among

medical doctors. The word autopsy is derived from the Greek word *autopsia* – to see with one's own eyes. It is the examination of the body of the dead primarily to determine the cause of death. Other aims are:

- To identify and characterise the extent of disease.
- To determine whether a particular medical or surgical treatment has been effective.
- In academic institutions for teaching and research purposes.
- Autopsy can also reveal the lifestyle and indulgences of an individual when alive, for example, fatty liver, cirrhotic liver may be signs that an individual was probably an alcoholic, though there are numerous other causes of fatty liver and liver cirrhosis.

Autopsy is the bedrock of morbid anatomy. Without autopsy morbid anatomy is naked and lonely. Most of the knowledge in clinical medicine is derived from post mortem examination of the dead. To date, the dead continue to pay some ransom for the living. It is the dead body, or cadaver that medical students dissect to acquire the knowledge of anatomy. In earlier centuries, dead bodies were often stolen for the purpose of dissection to acquire medical knowledge. There is a lot of contention in recent times in the western world about the retention of human organs after post mortem examination. The Alder Hey Hospital scandal in Liverpool, United Kingdom is a good example. The scandal which has dampened the morale and enthusiasm of paediatric pathologists is a prelude to the death of autopsy itself with serious consequences for mankind. One of these is that clinical diagnoses made ante mortem may not be verified, despite evidence showing more than one in ten may be wrong, even in the developed world.

I have performed series of autopsies on patients who had died of natural causes. The overwhelming majority of these cases are hospital patients who eventually died. It is improper to comment on this forum on many of the important autopsies handled by me. The reasons are obvious. Firstly many of these cases are still pending in court and involved important personalities. Secondly,

healed wounds must not be reopened. Again it is wisdom on our part to steer clear of unnecessary controversies. At this juncture, it is necessary to remind ourselves that the body, dead or alive belongs to the state (Campbell-Tiech A., 2002). This is actually borrowing from Divine ownership (Whether we live therefore, or die, we are the Lord's – Romans 14:8b). The implication for the practice of morbid anatomy is that the pathologist has the right to delay a body for burial until satisfactory post mortem examination is concluded. This is particularly true in medicolegal cases. The practice whereby relations of the dead harass and threaten pathologists with lawsuit for failure to release the bodies of their deceased relatives prematurely is uncalled for, and it shows a complete ignorance of the laws pertaining to the practice of autopsies.

In times of conflict it is common to find dead bodies brought to the morgue arrayed in war regalia decorated with charms and amulets calculated to insulate the wearer from gunshot and injuries. As a matter of fact, this was how wars were fought in Yorubaland in the 18<sup>th</sup> to 19<sup>th</sup> century (See War and Peace in Yorubaland edited by Akinjogbin A.). The wearing of charms and other "protective" armamentaria is not limited to warfare. Some commercial vehicle drivers are into the habit of hiding charms and animals such as tortoise underneath their dresses in their vain quest for protection against road traffic accident. Unfortunately the tortoise may survive while the owner of the tortoise dies.

Not all deaths contribute to medical knowledge. The picture below shows the body of a 24-year old female student in a polytechnic. She was stabbed with a knife on the chest after a brief argument on her blender, which she gave out to her assailant who happened to be a fellow student. Cases like this are more of interest to psychologists than to medical doctors.





**The picture shows the stab wound on the heart of the deceased.**

## **Cutting edge without a scalpel**

Is this the future that awaits autopsy? Is this a future in the instant? Reports on the decline in the rate of autopsies abound, even in Nigeria. It is generally agreed that there are times when autopsy is necessary. However, traditional autopsies are considered as too invasive procedures and may sometimes violate religious laws of the Jews and Muslims. Pathologists at Ife have often resorted to so-called "limited autopsy" in cases where relatives of the deceased are not willing to give consent to full autopsy, not necessarily based on their religious belief. Unfortunately, limited autopsies have serious limitations and vital questions may remain unanswered.

In the last few years scientists have developed the concept of virtual autopsy, or virtopsy, as is referred to in Switzerland. Virtual autopsy relies on computer tomography (CT) and magnetic resonance imaging (MRI) technologies to capture detailed X-rays and MRI images of the deceased body. A 3D image created by radiologists allows pathologists and medical examiners to examine the bones, tissues and organs of the body in order to determine the cause of death and the manner of death. Talk of morbid radiologists. Virtual autopsy is useful in cases of road traffic accidents in determining identity and cause of death in large scale disasters like hurricane and earthquake, when the body might have decomposed. It is very unlikely that this technology will be available for autopsies in Nigeria. Hospitals would not use MRI and CT scan on the dead that are already dead.

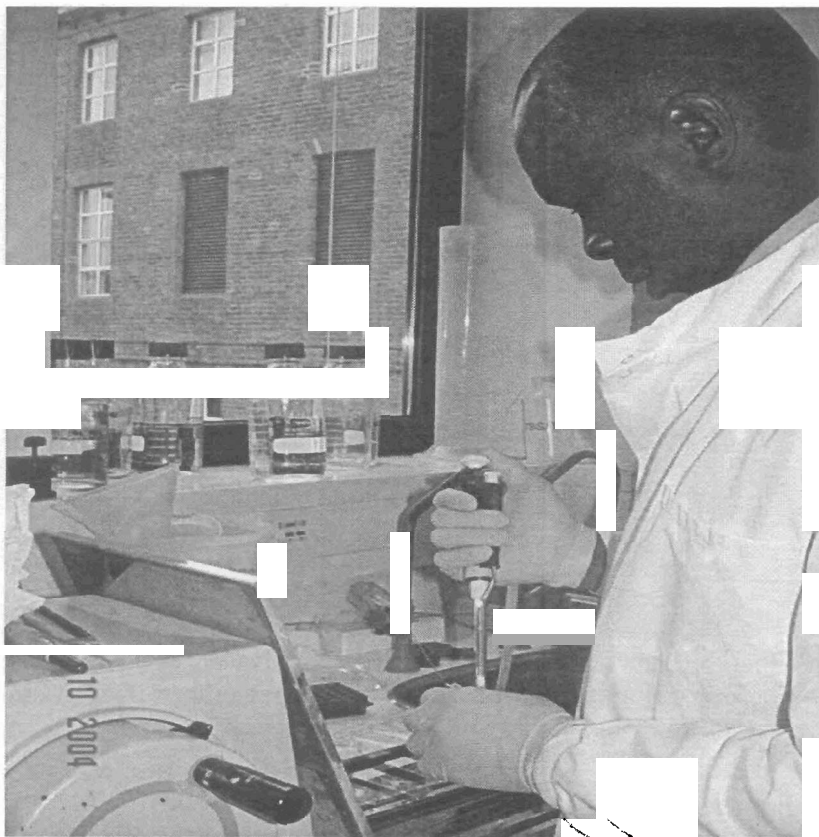
A new role is also emerging for the pathologist with the emergence of molecular autopsy. In view of the large number of cases of sudden cardiac deaths in young patients with no cardiac or coronary artery abnormalities, examiners have now focused on channelopathies. These are a group of diseases that develop secondary to genetic mutations which alter cardiac ion channel activity. Channelopathies have been identified in a number of autopsy-negative sudden cardiac deaths. Individuals with these

electrical diseases are vulnerable to fatal arrhythmias even at young age.

### **Human development**

The British Division of The International Academy of Pathology (BDIAP) is one of the international professional associations that has contributed and is still contributing to the development of morbid anatomy in Ife. I was the first pathologist to join the British Division not only in Ife but also in Nigeria. Since I became a member in 2004, the door has been thrown wide open to successive generations of resident doctors and consultants who have been sponsored to become members. Resident doctors benefit from the association more than other categories of pathologists. Every year, not less than two residents are sponsored to attend the annual scientific conference and also spend two weeks in a pathology department in the United Kingdom. Ife has been enjoying that monopoly for close to a decade now. Following a stint at the Kwame Nkrumah University of Science and Technology in Kumasi, Ghana, I was able to replace myself with a brilliant consultant pathologist who is a product of OAU and OAUTHC, Ife. His name is Dr. Nicholas Titiloye. Dr. Titiloye happens to be the current Head of Pathology in that foremost Ghanaian institution. He also heads the Pathology Department of the Komfo Anokye University Teaching Hospital in Kumasi. Dr. Titiloye has developed the Pathology Department in the university to a level far beyond imagination some few years ago.

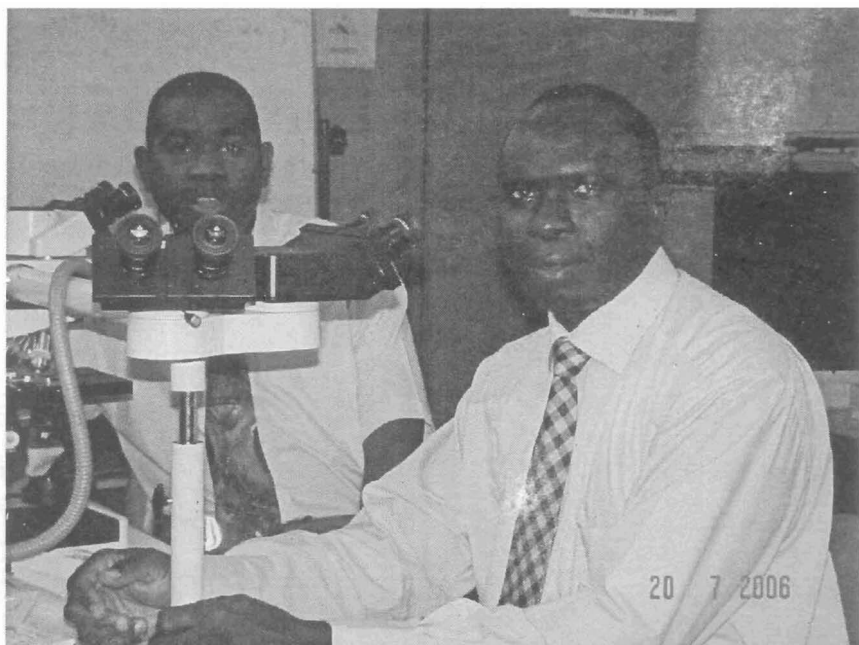




**At IHC laboratory, St. James' University Hospital, Leeds, UK.**

### **INCTR – Telepathology**

This is a new area in pathology that needs further development. Telepathology in Nigeria started in Ife with Professor Durosinmi's connection. It was launched by Nina Hurwitz and her team of INCTR experts at the seminar room of the Institute of Public Health, Obafemi Awolowo University on the 26<sup>th</sup> of January, 2010. The occasion was well attended with 41 delegates from many parts of Nigeria. The current Chief Medical Director of OAUTHC Professor Adejuyigbe provided funds for the purchase of the LEICA DMZ 750 microscope used for telepathology. Teleconsult, including teleconferencing through Skype with experts mainly in Europe went on very well.



**With Dr. Olorunda Rotimi at Histopathology Department, LGI, Leeds.**

### **The journey**

Like all academic journeys, it has been long, with periods of joy and uncertainties. I was born and grew up at Lafiaji area in Lagos Island. My primary school education was at St David's School, Lafiaji, Lagos. My early years in primary school were initially rough. Life in Lagos then was good with lots of entertainment mainly by different masquerades such as the eyo masquerades, Calabar masquerades, Ijebu masquerades and the igunnu. Father Christmas was a great attraction at Christmas. There were no kidnappers and everyone was his brother's keeper.

Secondary school education at Christ's School, Ado-Ekiti was a difficult period of my life. We had very good teachers. The students were also very proud of their school. Unfortunately, some of our seniors made life so terrible for their juniors. Junior students found solace in the popular apothegm at the time "seniority is not

forever". Christ's School was a center of academic excellence. I will never forget the School for all the good things it taught me and for my wonderful classmates.

I did my higher school education at the Federal School of Science popularly known as FSS at Victoria Island, Lagos. Life was good and tolerable at this time as I was also working. I was to proceed to the second year at A-level when the opportunity came to study medicine at the Soviet Union. I was on Federal Government scholarship throughout my university education. The Nigerian embassy in Moscow also provided extra stipends in pounds sterling for summer holiday which we normally spent criss-crossing central Europe and the United Kingdom. Life in the Soviet Union was very good and interesting. There was no problem with electricity or water supply, accommodation or transportation. It was like in the Elysium. Most of my years abroad were spent at the Donetsk State Medical Institute now Donetsk State Medical University in Ukraine. Donetsk is a beautiful city. I am yet to see the type of hostel I lived in as a medical student in Donetsk anywhere else apart from St Petersburg. I had a very good time as an undergraduate in Donetsk, for which I am very grateful to God for all these opportunities.

Things started getting rough and difficult during the Residency training at Ife. Residents were very poor in those days. The areas I like most in medicine are ophthalmology and haematology. After participating in the enucleation of the eye operation I abandoned the ambition of becoming an ophthalmologist. I decided to specialise in Morbid Anatomy because many doctors did not like that area of specialisation then. Thank God I made a right choice.

I thank the Lord who God Almighty who has given me the opportunity to give this lecture. I seize this opportunity to thank my loving and wonderful parents for training me in school, particularly primary and secondary schools. Without them I would have been an illiterate today. They also inculcated in me a large dose of discipline. I am indeed very grateful to them. I thank all my teachers and some of my seniors in Christ's School Ado-Ekiti.

Notable among my seniors is Dr. Sehinde Alo who found time to give me assignments regularly. I thank God that today he is also an orthopaedic surgeon in the United Kingdom.

I wish to appreciate all my lecturers in the university. They were disciplinarians of the highest order. Just forget about coming a minute late to class. Merely coughing during a lecture would land you in serious trouble. I will never forget to mention Professor Emmanuel Fagbamiye, a retired professor in education at the University of Lagos. It was through him that I got the Federal Government scholarship to study medicine. Professor Odesanmi facilitated my appointment as a Medical Training Fellow in Morbid Anatomy at Obafemi Awolowo University in October, 1987. I acquired some of my knowledge in forensic medicine through him. I am indeed very grateful to him. I am grateful to my immediate predecessors in Morbid Anatomy, Professor Segun Ojo and Professor Simeon Nwosu. They both taught me the rudiments of Morbid Anatomy as a Junior Resident in the Department.

Professor Akinsola of the Department of Medicine ignited my interest in nephropathology. It was he that organised my training in renal allograft rejection pathology at the University of Manchester, United Kingdom. He was also responsible for the one year Commonwealth Medical Fellowship tenure with the Laboratory Medicine Academic Group, University of Manchester. Dr. Olorunda Rotimi, a Senior Lecturer in histopathology at the University of Leeds and an alumnus of OAU is gratefully acknowledged. I got to know Professor Ken MacLenan, a professor in tumour pathology (lymphoma) through him. All my IHC studies were done in the research laboratory of Professor MacLenan at St James' University Hospital, Leeds. One of these was financed by the University Research Committee. Dr Rotimi was the one that sponsored me into BDIAP. This worthy alumnus of OAU has also donated many books and academic materials to the Department of Morbid Anatomy, OAU. I thank Professor M.A. for introducing me to the international scene in haematopathology. I wish to acknowledge with profound gratitude

all my research collaborators, in particular Professor Wasiu Olowu, Professor Oyeku Oyelami both of the Department of Paediatrics and Child Health and Professor Lara Orafidiya of the Faculty of Pharmacy.

An adage goes that behind every successful man is a woman, therefore, I wish to appreciate that woman, the Joy of my life, my wife Funmi, who stood by me through thick and thin, despite unemployment trend in the country. She left her promising job in Lagos to join me in Ife. I say thank you love. I also wish to appreciate my loving and beautiful children, Paula and Paul for their love, great companionship and support. I also thank my siblings, both in Nigeria and abroad for their love and encouragement. I thank my Father in the Lord Pastor Abiola Adeniran, Pastor Festus Adedokun, Pastor (Dr) Salawu, Prof. Jegede, Pastor Victor Bakare and my beloved brothers and sisters of the family of God, whose names are in the book of life.

## **Conclusion**

Mr Vice Chancellor Sir, knowledge about causation and effects of disease on the human body came to us through autopsy on the dead. Without controversy modern technological advancements have revealed hidden knowledge about diseases, their causes, treatment and control. Centuries ago it was survival of the fittest. Many scientists died at the prime of life due to one ailment or the other, most of which are now curable. Life expectancy has increased as a result of explosion in knowledge. However, there is a price to pay. This price may sometimes be in the form of adverse affects to our well being, and may be costly. The dead that are already dead continue to pay part of this ransom for those of us that are alive. They are our schoolmasters. To limit this ransom we must be aware of things that constitute danger to our well being in our environment and as much as possible avoid them. The International Union Against Cancer (UICC) has declared 4<sup>th</sup> of February world cancer day to raise awareness of cancer and encourage its prevention, detection, treatment and possibly cure.



The International Network for Cancer Treatment and Research (INCTR) is also pursuing this mission. The Well Woman Clinic at Eleiyele Community Health Centre under OAU Teaching Hospital is actively involved in the screening for breast cancer and cervical cancer. Screening for prostate cancer can also be done at the Chemical Pathology Department of OAUTHC. The University may wish to collaborate with the Teaching Hospital in establishing a modern cancer screening center with a well-equipped laboratory. A modern diagnostic center where immunohistochemistry and molecular biology techniques will be available should be established. The practice of travelling abroad to do quality research on our pathology samples must be reduced. We must commence bone marrow transplant (BMT) for lymphoma and other haematological malignancies at Ife. Dr. A.A. Oyekunle of the Department of Haematology and Immunology has undergone rigorous training in BMT in Germany and is a valued resource person in BMT nationwide. The use of various chemicals as herbicides and pesticides at home and on the farm must be with caution. Environmental and health impact assessment of the various cancer-predisposing agents in our environment must be conducted. The Federal Government must also empower the universities by making funds available for their development. I thank you all for your attention.

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